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Transrectal three-dimensional fetal volumetry and crown-rump length measurement during early gestation in mares: intra- and inter-observer reliability and agreement

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Inhalt

Zusammenfassung - Das Ziel dieser Studie war es, erstmals mittels einer transrektalen dreidimensionalen (3D) Ultraschalluntersuchung bei Stuten in der Frühgravidität das fötale Volumen (FV) zu bestimmen und mit der Scheitel-Steiss-Länge (SSL) zu vergleichen. Dazu wurden 149 Stuten am Tag 45 ± 1 der Trächtigkeit mit einem portablen Ultraschallgerät (Voluson® i, GE Healthcare, Zipf, Österreich) untersucht und von den Föten zwei- (2D) und dreidimensionale Bilder zur Messung der SSL und des FV angefertigt. Volumenmessungen erfolgten mit der Software Virtual Organ Computer-aided AnaLysis (VOCAL ™). Zur Überprüfung der Reproduzierbarkeit (Intra-Class-Correlation Coefficient = ICC; Bland-Altman-Analyse = LoA) wurden Messungen von zwei Untersuchern (A und B) je einmal wiederholt. Die SSL-Messung im 3D-Modus war besser reproduzierbar (ICC = 0.91 (0.88-0.94), P < 0.001; LoA = 0.13%, 95% CI: -7.45 bis +7.19) als die SSL Messung im 2D-Modus (ICC = 0.50 (0.36-0.61), P < 0.001; LoA = -1.54%, 95% CI: -23.29 bis +20.21). Sowohl die intra- als auch die interindividuelle Reproduzierbarkeit der FV-Messungen im 3D-Modus waren sehr gut. Zusammenfassend zeigen die Ergebnisse dieser Studie, dass die transrektale dreidimensionaler Sonographie ein sehr gut reproduzierbares Verfahren zur Bestimmung des Volumens von frühgraviden Pferdeföten darstellt.

Abstract – The aim of this study was to investigate if transrectal three-dimensional (3D) ultrasound is a reliable technique to measure equine fetal volume (FV) during early gestation in mares and to compare FV with crown-rump length (CRL) measurements. In total 149 warmblood mares were examined once transrectally on days 45 ± 1 of pregnancy with a portable 3D ultrasound device (Voluson® i, GE Healthcare, Zipf, Austria). Two-dimensional (2D) and three-dimensional CRL measurements were performed and FV was determined using Virtual Organ Computer-aided AnaLysis (VOCAL™) software. The 2D and 3D images were repeatedly analyzed by the same examiner (A) and by a second examiner (B) to analyze reproducibility (intraclass correlation coefficient = ICC; Bland-Altman's limits of agreement = LoA) of CRL and FV measurements. Repeated measurements of 3D CRL showed a higher reproducibility (ICC = 0.91 (0.88-0.94), P < 0.001; LoA = 0.13%, 95% CI: -7.45 to +7.19) compared to 2D CRL measurements (ICC = 0.50 (0.36-0.61), P < 0.001; LoA = -1.54%, 95% CI: -23.29 to +20.21). Intra- and inter-observer reproducibility of the 3D FV measurements was excellent. In conclusion, the results of this study showed that three-dimensional ultrasound in early gestation in mares is a reproducible technique to perform volume measurements in equine fetuses.

Key words: equine, three-dimensional ultrasound, VOCAL, fetal volume, crown-rump length, early gestation, intra- and inter-observer

1. Introduction

Three-dimensional (3D) ultrasonography in human obstetrics and perinatology is used in clinical practice, including fetal gender determination [1], detection of facial malformations [2], organ measurements [3], gestational age or birth weight prediction by fetal volume (FV) calculation [4, 5]. Three-dimensional ultrasonography allows scanning and studying fetal structures using the multiplanar view (the three orthogonal planes are displayed in this view). Currently, the most frequently used software to calculate organ or fetal volumes from 3D ultrasonographic datasets is Virtual Organ Computer-aided AnaLysis (VOCAL™, GE Healthcare, Zipf, Austria), which is validated in both *in vitro* [6, 7] and *in vivo* [8-12] studies in women. With VOCAL™ it is possible to obtain the fetal volume by manually outlining the contour of the fetus in different planes, while the 3D image is rotated about a fixed axis with a selected rotational angle.

Evaluation of the equine fetal size or growth has until now been assessed using two-dimensional (2D) measurements, mainly by measuring crown-rump length (CRL) [13-16], fetal aortic diameter [13, 17-19] or eye orbit diameter [13, 14, 17, 19, 20]. However, in women the weekly increase (at a gestational age from 6 to 13 weeks) is much higher for the fetal volume (5 to 35 fold) than for the CRL (2 to 4.5 fold) and the 3D volume measurement is less dependent on fetal attitude or movement than the CRL [21-23]. Taking this to account, 3D characterization of fetal size or growth is thought to be more reliable to predict the gestational age or identify early signs of impaired fetal growth than 2D measurements [21, 22, 24]. Thus, 3D ultrasound in equine reproduction could be an interesting tool for the assessment of fetal growth, as intrauterine growth retardation (IUGR) is associated with low birth weight, premature delivery or dysmaturity [25, 26] and consequently leads to perinatal death or equine neonatal illness [27-29] and can moreover affect postnatal growth [30-33].

The aim of the present study was to investigate reproducibility of FV measurements and CRL measurements obtained by 2D and 3D ultrasound during early gestation (Day 45 ± 1) in mares. To assess reproducibility of 3D measurements inter- and intra-observer repeatability analyses were performed.

2. Materials and methods

2.1. Animals

During the breeding season of 2016 a total of 153 warmblood mares were examined on a stud farm in the northern part of Germany. The age of the fetus was determined according to the day of ovulation (= Day 0). Furthermore, it was taken into account whether the embryo was transferred to a recipient mare or it developed in its genetic mother after insemination. On Day 16 mares were examined for pregnancy, using ultrasonography or on Day 14 if they had a risk of carrying twins. If a twin pregnancy was diagnosed, one embryonic vesicle was crushed.

2.2. Three-dimensional ultrasonography

Two- and three-dimensional ultrasonography was performed transrectally using the portable ultrasound device Voluson® i (GE Healthcare, Zipf, Austria) equipped with a 3 to 9 MHz microconvex transducer (RNAs5-9-RS) which was protected by a rectal sleeve. Each mare was examined once transrectally by a single examiner at day 45 ± 1 of gestation. If necessary the mares were sedated once with 0.01-0.02mg/kg iv detomidinhydrochlorid (Domosedan®, Pfizer Animal Health, Elsene, Belgium). As soon as the fetus was localized by using 2D mode, three CRL measurements were acquired and the duration of the examinations was recorded. Afterwards, the examiner changed to 3D mode and started again to record the time of measurements. The sector angle and penetration depth were optimized for each fetus. The acquisition of 3D images was continued until three datasets were obtained. The 2D and 3D images were initially stored on the hard drive of the ultrasound device and transferred once weekly on an external hard drive.

2.3.Determination of volume und crown rump length of the fetuses

A mean CRL value was calculated from the three 2D pictures ($CRLA_{2D}$). Image quality of the 3D images was evaluated based on the presence or absence of motion artefact, definition of the fetal contour (blurry or sharp-edged) and the degree of uterine wall contact of the fetus. From the stored 3D images the best, in terms of image quality, was chosen for further assessments. Three-dimensional CRL was assessed by evaluating the sagittal plane of the fetus in multiplanar view using 4DView™ software v.14 Ext.2 (GE Healthcare, Zipf, Austria. This procedure was repeated three times to calculate the mean 3D CRL ($CRLA_{3D}$), which was used for further analysis. Volumes were obtained with the extended software Virtual Organ Computer-aided AnaLysis (VOCAL™, GE Healthcare, Zipf, Austria). The fetus was positioned in a sagittal view in plane C so that the rotational axis could be set along the longest axis of the fetus. This procedure was found to be optimal in retaining a good orientation of the fetus during the rotational analysis [10]. Subsequently, the fetus was rotated 180° with two variations of rotational angles; one with an angle of 6° and one with 30°. During the 180° rotation, the fetal head and trunk (limbs were excluded) was manually contoured in each plane (30 planes for 6° and 6 planes for 30°) and the software calculated the FV in cm^3, resulting in FVA_6 (6° rotational angle) and FVA_{30} (30° rotational angle) (Figure 1). A dataset of 60 3D images was chosen in order to perform repeatability studies. Examiner A repeated the FV measurement with the same technique at a rotational angle of 30° ($FVAR_{30}$) and 6° ($FVAR_6$). For the inter-observer repeatability analysis of CRL and FV (30° rotational angle) the same dataset of images (n = 60) was analyzed from a second examiner (B), resulting in $CRLB_{3D}$ and FVB_{30}. For each measurement the duration was recorded from beginning to completion of CRL or FV measurement.

2.4.Statistical methods

Statistical analysis was performed using SPSS version 23.0 (SPSS Inc., Chicago, Il, USA) and $P < 0.05$ was considered statistically significant. The normality of the values was tested using Shapiro Wilk test. The paired-sample t-test was performed to test for differences of measured values. In cases where the distribution deviated from normal, the Wilcoxon signed-ranks test was used [34]. To describe the relation between CRL and FV measurements, THE Pearson correlation coefficient (r) was calculated. Inter- and intra-observer reliability (for CRL and FV) as well as the inter-method reliability (comparing FVA_{30} and FVA_6) were evaluated using intraclass correlation coefficient (ICC, two-way mixed, absolute agreement), where ICC > 0.75 is consistent with a high reliability [35]. To evaluate CRL reliability and agreement of each method (2D or 3D), the first and the third measurements were used. The inter-method, inter- and intra-observer agreement were investigated based on the method proposed by Bland-Altman by plotting the percentage difference (i.e. 100 x (first measurement-second measurement)/average) against the average, and calculating the respective 95% limits of agreement (95% LoA) and 95% confidence intervals (95% CI) [36-38].

3. Results

Four mares (2.7%) were excluded retrospectively due to poor image quality, resulting in a complete image dataset of 149 warmblood mares (n = 149; 94 Oldenburg international, 22 Oldenburg, 11 Zangersheide, 8 Hanoverian, 5 Selle francais, 4 Mecklenburger, 3 Holsteiner, 1 Westphalian, 1 Anglo-Arabian). The exclusion of the 3D images was due to blurry fetal edges (2%, n = 3) or the fetus lied partially at the uterine wall to an unacceptable degree (0.7%, n = 1). Results are given in mean ± SD and range (minimum, maximum). The mean age of the mares was 10 years (10 ± 4; 3, 22 y), with a parity of 5 (5 ± 3; 0, 12). The mares were examined on days 44 (n = 34), 45 (n = 34) and 46 (n = 34) of gestation, respectively.

The mean CRL and FV measurements are listed in *Tables 1* and *2*, respectively. The $CRLA_{3D}$ was 0.1 ± 0.21 cm longer than the $CRLA_{2D}$ measured by examiner A ($P < 0.05$). Within the measurements of examiner A no differences between the measured FV were found regardless of the applied rotational angle ($P > 0.05$). When measurements between the two examiners were compared, examiner A measured the 3D CRL longer ($P < 0.05$) and the FV smaller compared to examiner B ($P < 0.05$).

Results of the repeatability analysis including ICC values and Bland-Altman's LoA are shown in *Table 3*. Repeatability analysis revealed poor reliability between $CRLA_{2D}$ and $CRLA_{3D}$ (inter-method). In contrast, volume calculations with different rotational angles (i.e. 6° and 30°) showed high reliability and agreement (inter-method) and a reduction of the rotational angle (6°) did not result in a higher ICC value or a narrower 95% LoA. The highest ICC value was seen for the intra-observer FV analysis with a 30° rotational angle (FVA_{30} - $FVAR_{30}$). Similarly, a good measurement agreement was observed for the intra-observer FV measurement with a 30° rotational angle (LoA width of 20.6%). Inter-observer ICC was poor for 3D CRL measurements ($CRLA_{3D}$-$CRLB_{3D}$) but high for FV measurements (FVA_{30}-FVB_{30}). Inter-observer agreement appeared to be better in CRL measurements (36.3%) compared to a relatively wide LoA (66.1%) for FV measurements. Correlation between CRL and FV measurements was the highest for $CRLA_{3D}$ and FVA_6 ($r = 0.83$, $P < 0.001$), followed by $CRLA_{3D}$ and FVA_{30} ($r = 0.78$, $P < 0.001$). The correlations of $CRLA_{2D}$ with FVA_{30} and FVA_6 were only moderate (FVA_{30} $r = 0.55$ and FVA_6 $r = 0.57$, $P < 0.001$).

The 2D examination including localization of the fetus and CRL measurements in 2D mode took about 2 minutes (*Table 4*). The extra time needed to obtain 3D images of the fetus was in average 2 minutes and 37 seconds. When FV were measured on a personal computer, the duration of the FVA_{30} measurement (with only 6 planes analyzed) was shorter than the duration of FVA_6 measurement (with 30 planes analyzed) ($P < 0.001$). Examiners A and B needed the same amount of time to calculate FV ($P > 0.05$).

4. Discussion

The 3D method was successfully applied in mares during the second month of pregnancy. We analyzed intra- and inter-observer, as well as inter-method reliability and agreement of 2D and 3D CRL measurements and FV calculations with differing rotational angles.

The most frequently used software to calculate organ or fetal volumes from 3D ultrasonographic datasets is VOCAL™, but despite of its frequent use, it also has limitations: (1) overestimation of true volumes due to limited resolution [7, 39]; (2) unfeasibility to include limbs in the total FV, as the software is not able to measure several objects in one image [22-24]; (3) exact placement of the fetal contour is subject to individual variation [9, 39]; (4) blurred edges in small objects or deeper layers make it difficult to clearly identify fetal contours [9, 40]; (5) duration to perform the measurement can be quite long depending on rotational angle [6, 7, 10].

There is a big discrepancy in literature whether limbs should be included in the measurement of the fetal volume assessment or not. In women, fetal extremities represent a significant proportion of the size of the fetal body (approximately 5-10%) and therefore should not be excluded [41]. On the other hand, there are always planes in which the limbs appear disconnected from the trunk due to the rotation of the fetus about the fixed axis. Thus, inclusion of fetal limbs with VOCAL™ is impracticable [11, 24]. In horses there is no actual data on how much the limbs account for the total size of the equine fetus in early gestation. In the current study limbs were only visible as small buds and were excluded.

We compared fetal volume measurements with rotational angles of 6° and 30°, with the fetus being rotated about its longest axis, as previously suggested by Barra et al. in human fetuses (2013) [10]. An *in vitro* study by Raine-Fenning et al. (2003) showed an increased reliability for irregular shaped objects (phantoms) when small rotational angles (of 6° or 9°) were applied [7]. However our results support the findings of Barra et al. (2013), showing that the application of a small rotational angle does not increase reliability. This could be explained by the positioning of the chosen rotational axis through the longest axis of the fetus, where the changes between the successive planes seemed to be less prominent [10]. Additionally, the exclusion of the fetal limbs allowed the examination of a relatively simple and less irregular structure (fetal head and trunk).

The high reliability of equine FV measurements in the present study is in accordance with previous publications of volume measurements in human fetuses at a similar gestational age (intra-observer ICC (30°): 0.98 - 0.996) [10, 42]. The interpretation of the Bland-Altman's LoA is defined by its purpose: It simply quantifies the bias and does not define whether the agreement is sufficient for clinical use [36-38]. According to Barra et al. (2013) LoA should not be wider then ± 20% (LoA width < 40%) [10] in clinical trials, which was the case for all measurements of this study, except for the repeated 2D CRL measurements and inter-observer FV calculations. The wide LoA for the inter-observer FV calculations could be attributed to the examiners' subjective decision where exactly to draw the contour around the fetus. To our opinion this appears to be the main limitation for VOCAL™ software. Additionally, lack of experience of the examiners could be a reason for the discrepancy in the measured volumes, as both examiners were involved for the first time with this technique. Nevertheless, higher bias and variance are expected when two measurements are compared with different methods (inter-method) or from different examiners (inter-observer) [37].

Four of the 3D images were excluded retrospectively due to poor image quality. Limited resolution in 3D images might be due to movement artefacts, which are a lot more difficult to avoid in equine practice than in human medicine. Thus, an unsuitable fetal position (e.g. adjacent to uterine wall) and the mare's movements, including skin twitching, breathing and peristaltic gut movements might be the main reasons for a moderate or poor 3D image quality.

Three-dimensional ultrasound requires an additional examination time of approximately two and a half minutes, which is a minimal expenditure of time in terms of recording a 3D image. On the other hand the offline evaluation of the FV is a time consuming procedure and the duration of the volume calculation depends on the chosen rotational angle. Meaning, a reduction in the rotation angle results in a longer analyzation time, because more planes have to be evaluated [7]. Mean FV calculation time is reported for human fetus measurements and ranges between approximately one to two minutes [10, 43] and two to five minutes [8-10] for 30° and 9° rotational angles, respectively. No comparative time measurement was found in literature regarding the calculation of a FV with 6° rotational angle in human fetuses. Overall, the calculation of the FV can be a time consuming technique depending on the used rotational angle and is not feasible during an ambulatory visit.

The mean 2D and 3D CRL obtained in this study was about 1 cm longer than the ultrasonographically assessed CRL reported in literature for these days of pregnancy [14, 15]. Ginther (1995) described that CRL measurements may have been underestimated, because the longest axis of the fetus may not have been found in some cases [15]. However, our CRL measurements are similar to the ones reported by Franciolli et al (2011), who macroscopically measured CRL (day 40-47 of gestation: 3.6 - 4.6cm) in equine fetuses collected from the abattoir [44]. This finding supports the greater accuracy of 3D ultrasound, where through modification of the 3D image the actual longest sagittal plane of the fetus can be determined post-examination. This enables the examiner to perform a more precise measurement without time pressure. However, it is unclear why our 2D CRL measurements exceeded the reference values for CRL reported by others [14, 15]. The CRL measurements obtained using 2D and 3D mode differed in the present study. The clinical meaning of an approximately 1 mm (3.1%) difference should be further investigated. Three-dimensional CRL measurements showed a high reliability and agreement, in contrast to the repeated 2D CRL measurements. Thus, 3D ultrasound is superior to 2D in determining CRL.

In early human gestation the weekly increase in FV is much higher than the advancement of CRL and the 3D volume measurement is less dependent on fetal attitude than the CRL [21-23]. Therefore, volume calculations are thought to be more reliable to predict the gestational age or identify early signs of impaired fetal growth [21-23]. Thus, three-dimensional ultrasound is a promising area of research with a variety of practical applications. Future studies should clarify whether growth retardation in the equine fetus could be assessed by measuring equine FV in early gestation; and if FV could be a predicting factor for low birth weight in foals.

5. Conclusions

In conclusion, the 3D method was successfully applied during early pregnancy in mares and various CRL and 3D measurements could be acquired. Our study showed a high level of intra-observer reliability and agreement indicating that fetal volume measurement during early pregnancy in mares is a feasible technique for equine fetal size measurement. The main limitation of equine FV measurements performed with VOCAL™ software appears to be attributed to the examiners' subjective decision where exactly to draw the contour around the fetus. We therefore recommend specific training for examiners. Regarding CRL measurements, the approach by 3D ultrasound seemed to be superior to the conventional 2D measurements. Furthermore, reduction of possible sources of movement artefacts is essential for good quality images.

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7. Declaration of interest

None declared.

8. References

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9. Figures and tables

Table 1 Crown-rump length (CRL) measured by two examiners (A and B) using two-dimensional (2D) and three-dimensional (3D) ultrasound

CRL (cm)	Mean ± SD (range)
$CRLA_{2D}$ (n = 149)	3.18 ± 0.25^{a} (2.39 - 3.87)
$CRLA_{3D}$ (n = 149)	3.28 ± 0.25^{b} (2.58 - 3.99)
$CRLB_{3D}$ (n = 60)	3.12 ± 0.29^{c} (2.32 - 3.79)

$CRLA_{2D}$: 2D CRL measurement performed by examiner A, **$CRLA_{3D}$:** 3D CRL measurement performed by examiner A, **$CRLB_{3D}$:** 3D CRL measurement performed by examiner B.
$^{a, b, c}$: Values with different letters within the same column denote significant differences ($P < 0.05$).

Table 2 Fetal volume (FV) measured by two examiners (A and B) using three-dimensional (3D) ultrasound

FV (cm^3)	Mean ± SD (range)
FVA_{30} (n = 149)	3.99 ± 0.79^{a} (2.32 - 6.32)
$FVAR_{30}$ (n = 60)	4.09 ± 0.79^{a} (2.61-6.03)
FVA_{6} (n = 149)	3.96 ± 0.77^{a} (2.44 - 6.31)
$FVAR_{6}$ (n = 60)	4.07 ± 0.83^{a} (2.57 - 6.01)
FVB_{30} (n = 60)	4.47 ± 1.01^{b} (2.611 - 7.623)

FVA_{30}: FV measurement with a rotational angle of 30° performed by examiner A and **$FVAR_{30}$:** repeated measurement, **FVA_{6}:** FV measurement with a rotational angle of 6° performed by examiner A and **$FVAR_{6}$:** repeated measurement, **FVB_{30}:** FV measurement performed by examiner B with a rotational angle of 30°.
$^{a, b}$: Values with different letters within the same column denote significant differences ($P < 0.05$).

Table 3 Intra-observer, inter-method and inter-observer reliability and agreement analysis for the crown-rump length (CRL) and the fetal volume (FV) measurements. Displayed are the intra-class correlation coefficients (ICC) with their 95% CI and limits of agreement (LoA) widths for relative differences (% differences) with their 95% CI.

Mode of repeatability analysis	Analyzed measurements	ICC (95% CI)	Mean difference in % (95% LoA with 95% CI)
Intra-observer	$CRLA_{2D}$ (n = 149)	0.50 (0.36 - 0.61)	-1.54 (-23.29 to 20.21)
Intra-observer	$CRLA_{3D}$ (n = 149)	0.91 (0.88 - 0.94)	0.13 (-7.45 to 7.19)
Inter-method	$CRLA_{2D}$-$CRLA_{3D}$ (n = 149)	0.61 (0.42 - 0.73)	-3.02 (-18.38 to 12.34)
Inter-observer	$CRLA_{3D}$-$CRLB_{3D}$ (n = 60)	0.56 (0.04 - 0.78)	-6.75 (-23.08 to 13.18)
Intra-observer	FVA_{30}-$FVAR_{30}$ (n = 60)	0.98 (0.97 - 0.99)	0.18 (-10.11 to 10.48)
Intra-observer	FVA_{6}-$FVAR_{6}$ (n = 60)	0.95 (0.91 - 0.97)	0.31 (-15.96 to 16.59)
Inter-method	FVA_{30}-FVA_{6} (n = 149)	0.94 (0.92 - 0.96)	0.58 (-15.66 to 16.82)
Inter-observer	FVA_{30}-FVB_{30} (n = 60)	0.85 (0.67 - 0.92)	-6.71 (-39.78 to 26.36)

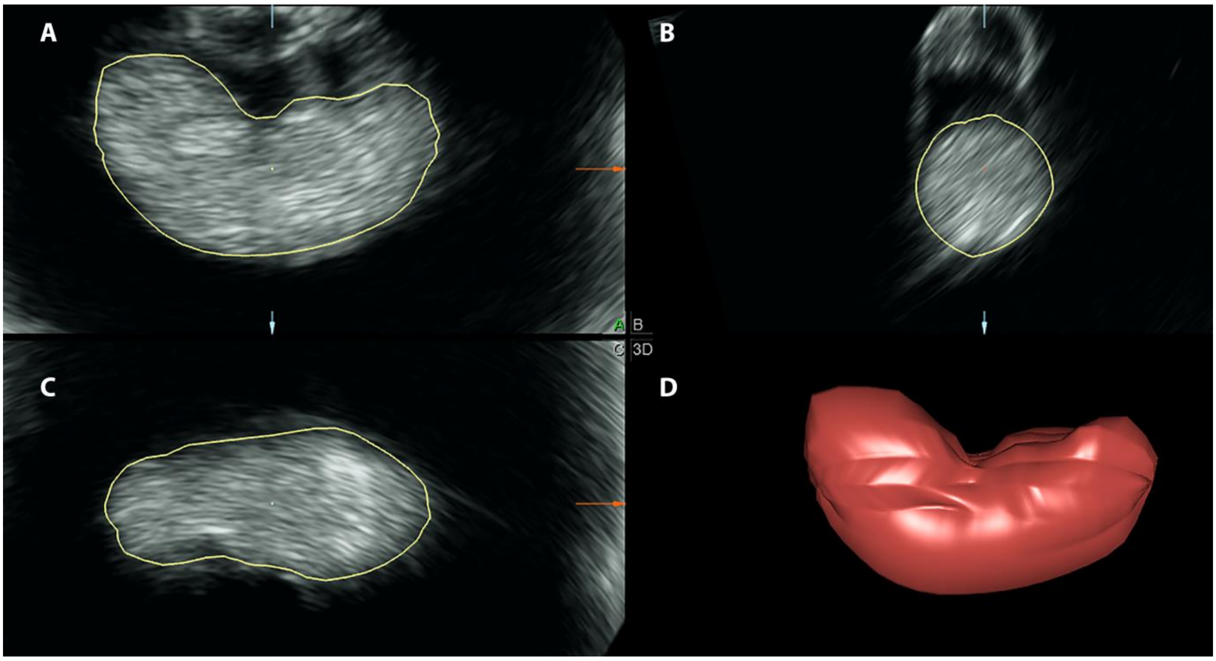
Intra-observer $CRLA_{2D}$: compares the first and the third 2D CRL measurements; **Intra-observer $CRLA_{3D}$:** compares the first and the third 3D CRL measurements; **FVA_{30}- $FVAR_{30}$:** intra-observer repeatability analysis with 30° rotational angle; **FVA_{6}-$FVAR_{6}$:** intra-observer repeatability analysis with 6° rotational angle; **$CRLA_{3D}$-$CRLB_{3D}$:** inter-observer (examiners A, B) repeatability analysis of 3D measured CRL; **FVA_{30}- FVB_{30}:** inter-observer (examiners A, B) repeatability analysis with 30° rotational angle; **$CRLA_{2D}$- $CRLA_{3D}$:** repeatability for the CRL measured with two different methods (2D and in 3D mode); **FVA_{30}- FVA_{6}:** Repeatability analysis between two different methods of FV measurement (6° and 30° rotational angle).

Table 4 Duration of the 2D (two-dimensional) and 3D (three-dimensional) ultrasound examinations and the fetal volume measurements with VOCAL™. Time is given in minutes:seconds, displayed are the mean ± SD, minimum and maximum time required.

	2D Examination	3D Examination	Duration FVA_{30}	Duration FVA_{6}	Duration FVB_{30}
Mean ± SD	01:56 ± 01:11	02:37 ± 01:21	03:30 ± 00:46[a]	08:10 ± 01:05[b]	03:20 ± 01:20[a]
Minimum	00:31	00:47	02:17	05:56	01: 48
Maximum	06:16	08:45	06:05	11:52	07:29

FVA_{30}: FV measurement with a rotational angle of 30° performed by examiner A; **FVA_{6}:** FV measurement with a rotational angle of 6° performed by examiner A; **FVB_{30}:** FV measurement performed by examiner B with a rotational angle of 30°.
[a, b]: Values with different letters within the same row denote significant difference (P < 0.001).

Figure 1 Multiplanar view of the three-dimensional (3D) head and trunk volume of a 45 day old fetus as assessed by VOCAL™



A) sagittal plane; B) transversal plane; C) frontal plane; D) reconstructed 3D fetal volume.

10. Curriculum Vitae

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